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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,811	06/08/2007	Mark I. Greene	UPN-5240	2423

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EXAMINER	
TUNG, JOYCE	
ART UNIT	**PAPER NUMBER**
1637	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,811	GREENE ET AL.	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,8,9 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 8-9 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed 1/12/10 to the Office action has been entered. Claims 1-3, 8-9 and 28 are pending.

1. The rejections of claims 4-7 under rejected under 35 U.S.C. 103(a) as being unpatentable over Eberwine et al. (5,922,553, issued Jul. 13, 1999) in view of Eberwine (7,115,371, issued Oct. 3, 2006) and Waggoner (5627027, May 6, 1997) and Sano et al. (5,665,539, issued Sep. 9, 1997) as applied to claims 1-3 and 8-9 above, and further in view of Yamane et al. (6,207,378, issued Mar. 27, 2001) are withdrawn because of the cancellation of the claims.

2. Claims 1-3, 8-9 and 28 remain respectively rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 7,524,628, issued Apr. 28, 2009, claims 1-16 of U.S. Patent No. 7,045,286, issued May 16, 2006 in view of Eberwine et al. (5,922,553, issued Jul. 13, 1999), claims 1-2, 4-6, 8-12, 14-16, 18-24 of U.S. Patent No.7,361,464, issued Apr. 22, 2008, and claims 1-3, 5-7, 9, 11-14, 16-18, 20, 22-24 of U.S. Patent No. 7,341,831, issued Mar. 11, 2008 because the terminal disclaimers were not filed.

3. Claims 1-3, 8-9 and 28 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Eberwine et al. (5,922,553, issued Jul. 13, 1999) in view of Eberwine (7,115,371, issued Oct. 3, 2006), Waggoner (5,627,027, May 6, 1997), and Sano et al. (5,665,539, issued Sep. 9, 1997).

Eberwine et al. ('553). disclose a method, which is for detecting a selected protein by immuno aRNA (See column, 2, lines, 37-50). The presence and quantity of labeled RNA transcript is indicative of the amount of selected protein present (See column 4, lines 33-36 and

columns 7-8, claims 1-2). In the method, a first antibody targeted to the selected protein is immobilized to a solid support. A RNA-promoter driven cDNA sequence is covalently coupled to a second antibody, which binds to the selected protein (See column 2, lines 37-51). The cDNA is double stranded (See column 5, lines 34-35) for use as a template for T7 RNA polymerase (see column 4, lines 41-42). The technique of a RNA synthesis is explicitly disclosed (See column 3, lines 9-24). First strand synthesis proceeds with the addition of AMV-reverse transcriptase (See column 4, lines 50-51). The solid support can be microtiter plates and beads (see column 4, lines 17-20).

Eberwine et al ('553) do not disclose a monoclonal antibody which binds to a selected epitope comprising a universal epitope.

Eberwine et al. ('371) disclose a method for detecting molecules expressing a selected epitope in a sample (see column 2, lines 47-49). The method applies a single chain Fv or CDR which contains a universal epitope such as hemagglutinin HA tag or polyhistidine tag (see column 8, lines 64-67). A single monoclonal antibody or single chain Fv coupled with a ds-DNA is the epitope detector. The efficacy of a universal epitope detector is demonstrated. After T7 polymerase amplification, specific bands from lysates of 10^{-6} dilution are detected (see column 9, lines 1-12).

One of ordinary skill in the art would have been motivated to apply a monoclonal antibody which binds to a selected epitope comprising a universal epitope as taught by Eberwine et al. ('371) because the efficiency for detection is increased (see column 9, lines 1-12). It would have been prima facie obvious to apply a monoclonal antibody which binds to a selected epitope comprising a universal epitope.

The above-cited references do not disclose the step (d) of claim 1 of contacting an amplified oligonucleotide with a fluorescence dye which stains RNA amplification product.

Waggoner discloses that cyanine dye can be used to attach to fragments of DNA or RNA to identify the presence and quantity of a specific nucleotide sequence in samples of DNA or RNA (See column 8, lines 51-56).

One of ordinary skill in the art at the time of the instant invention would have been motivated to apply a fluorescent dye, such as cyanine dye to stain unlabeled amplified RNA of Eberwine et al. for detecting and/or quantifying molecules expressing a selected epitope in a sample because as indicated by Waggoner, cyanine dye is a highly light-absorbing dye for use with nucleic acids and can be used for detection and quantification in very low amounts (See column 4, lines 35-45) It would have been prima facie obvious to apply cyanine dye for detecting or quantifying molecules expressing a selected epitope in a sample.

None of the references above discloses a biotinylated monoclonal antibody and a biotinylated oligonucleotide which form antibody and oligonucleotide complex via streptavidin.

Sano et al. disclose a linker which is a biotinylated nucleic acid marker cross-linked to biotinylated antibody by streptavidin or avidin (see column 4, lines 27-31).

One of ordinary skill in the art would have been motivated to apply the linker as taught by Sano et al. because the method of Sano et al. is a very sensitive method for detecting an antigen (see column 1, lines 38-39). It would have been prima facie obvious to use a biotinylated monoclonal antibody and a biotinylated oligonucleotide which form antibody and oligonucleotide complex via streptavidin.

The response argues that Eberwine and Sano fail to teach the linear quantification of the molecule comprising the selected epitope by using a fluorescent stain to label the RNA amplification product. However, the claim does not require an RNA amplification product which is labeled. Nevertheless Eberwine et al. (553) disclose that the presence and quantity of labeled RNA transcript is indicative of the amount of selected protein present (See column 4, lines 33-36 and columns 7-8, claims 1-2). Sano et al. also disclose that the quantitation of PCR products provides the estimation of the number of antigens (see column 4, lines 15-16).

The response further argues that Waggoner discloses the use of *cyanine-labeled RNA probes* for hybridization to a target sequence, and not the staining of *unlabeled* amplified RNA with cyanine dye. However, Waggoner discloses that cyanine dye can be used to attach to fragments of DNA or RNA to identify the presence and quantity of a specific nucleotide sequence in samples of DNA or RNA (See column 8, lines 51-56). The attachment of cyanine dye to DNA or RNA fragments is interpreted as fluorescent dye staining a DNA or RNA fragment.

The response also argues that the instant invention does not involve covalent attachment of cyanine dye, but rather the intercalation of the dye in the nucleic acid (see pg. 26 Example 1 of the specification). However, the claims are read in light of the specification, limitations from the specification cannot be improperly read into the claims.

Based upon the limitations above, the rejection is maintained.

NEW GROUNDS OF REJECTION NECECISTATED BY THE AMENDMENT

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-3, 8-9 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The newly added limitation "that is not labeled with a radioactive label or a fluorescent label" does not have support in the specification. Thus, it constitutes new matter.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637

/Joyce Tung/
Examiner, Art Unit 1637
April 5, 2010